

Protein folding, anisotropic collapse and blue phases

E. Pitard, T. Garel and H. Orland

Service de Physique Théorique

CE-Saclay, 91191 Gif-sur-Yvette Cedex

France

(February 1, 2008)

We study a homopolymer model of a protein chain, where each monomer carries a dipole moment. To mimic the geometry of the peptidic bond, these dipoles are constrained to be locally perpendicular to the chain. The tensorial character of the dipolar interaction leads naturally to a (tensorial) liquid crystal-like order parameter. For non chiral chains, a mean field study of this model shows that a classical θ collapse transition occurs first; at lower temperature, nematic order sets in. For chiral chains, an anisotropic (tensorial) collapse transition may occur before the θ temperature is reached: the ordered phase can be described as a “compact phase of secondary structures”, and possesses great similarities with the liquid crystal blue phases.

Accepted for publication in:

Saclay, SPhT/97-025

“J. de Physique I”

PACS: 61.41; 87.15.Da; 64.70.Md

I. INTRODUCTION

Proteins are chiral heteropolymers, made out of twenty species of monomers (aminoacids). Natural proteins have the property of folding into an (almost) unique compact native structure, which is of biological interest [1,2]. The compactness of this unique native state is largely due to the existence of an optimal amount of hydrophobic aminoacid residues [3], since these biological objects are usually designed to work in water. The existence of secondary structures [4] plays a predominant role in the existence of the unique native state. From a theoretical point of view, one may either emphasize the heterogeneous character of these biopolymers [5], or choose to focus on the more crystalline-like secondary structures (α -helices and β -sheets). In the first approach, folding is identified to a freezing transition; in the second approach, that we follow in this paper, the folding transition is more like a gas-solid transition. Previous studies along the latter path made use of simplified lattice models [6]. We consider here a microscopic continuous model of a homopolymer chain, where each monomer carries a dipole moment. The rationale for this choice is clear if one interprets the chemist's hydrogen bonds as the interaction between electrostatic dipoles (the secondary structures approximately corresponding to the classic dipole equilibrium positions). The dipolar moment of a *CONH* is $p_0 \simeq 3.6\text{D}$, yielding a typical dipolar temperature (temperature below which dipolar effects become relevant) of $T_D = \frac{p_0^2}{4\pi\epsilon_0\epsilon_r d^3}$ where ϵ_r is the relative dielectric constant of the medium, and d is a typical distance between dipoles. The electrostatics of proteins in water is a somewhat controversial issue [7], so we will content ourselves with an estimate of T_D in the native state. It is then appropriate to take $\epsilon_r \sim 5$ [7]. With $d \sim 3.8 \text{ \AA}$ [1], we find $T_D \simeq \frac{2000}{\epsilon_r} \simeq 400K$, so that dipolar effects may play a crucial role in the energetics of the folding (or unfolding) transition. The spatial range of the dipole-dipole interaction can be finite or infinite: its angular dependence (or tensorial character) is the crucial issue of this paper. To make a closer connexion with proteins, we assume that the dipole moments are constrained to be perpendicular to the chain. In this way, a monomer can be thought of as linking two successive C_α carbon atoms, and its dipole moment rep-

resents the peptid *CONH* dipole. A finite range of the dipolar interaction may further describe the finite range character of the hydrogen bonding interactions. The Hamiltonian of the model then reads

$$\beta\mathcal{H} = \frac{v_0}{2} \sum_{i \neq j} \delta(\vec{r}_i - \vec{r}_j) + \frac{\beta}{2} \sum_{i \neq j} \sum_{\alpha, \gamma} p_i^\alpha G_{\alpha\gamma}(\vec{r}_i, \vec{r}_j) p_j^\gamma \quad (1)$$

In equation (1), $\beta = \frac{1}{T}$ is the inverse temperature, v_0 is the excluded volume, \vec{r}_i denotes the spatial position of monomer i ($i = 1, 2, \dots, N$), and \vec{p}_i its dipole moment. If necessary, three body repulsive interactions may be introduced, to avoid collapse at infinite density. The (infinite range) dipolar tensor reads

$$G_{\alpha\gamma}(\vec{r}, \vec{r}') = A \frac{1}{|\vec{r} - \vec{r}'|^3} (\delta_{\alpha\gamma} - 3v_\alpha v_\gamma) \quad (2)$$

with $v_\alpha = \frac{(\vec{r} - \vec{r}')_\alpha}{|\vec{r} - \vec{r}'|}$ and A is a prefactor containing the dielectric constant of the medium. The dipolar interaction (2) is cut-off at small distances ($|\vec{r} - \vec{r}'| < a$) and may also be cut-off at large distances by an exponential prefactor. The partition function of the model (1) is given by:

$$\mathcal{Z} = \int \prod_i d\vec{r}_i d\vec{p}_i \delta(|\vec{r}_{i+1} - \vec{r}_i| - a) \delta(|\vec{p}_i| - p_0) \delta(\vec{p}_i \cdot (\vec{r}_{i+1} - \vec{r}_i)) \exp(-\beta\mathcal{H}) \quad (3)$$

In equation (3), a denotes the Kuhn length of the monomers, and p_0 is the magnitude of their dipole moment. The third δ -function restricts the dipole moment to be perpendicular to the chain; this mimics the free rotation of the *CONH* dipole around the $C_\alpha - C_\alpha$ “virtual bond”. As it stands, this partition function is not easy to evaluate. In particular the constraint of fixed length dipoles is not easy to implement. We have therefore studied the constrained dipolar chain in (i) in the framework of the virial expansion, with fixed length dipoles (ii) in the framework of a Landau theory, where we replace the fixed dipole length by a Gaussian distributed length.

II. THE VIRIAL APPROACH

Since the virial extension is quite familiar in the field of polymeric liquid crystals [8], we will be rather sketchy in our presentation. Starting from equations (1-3), we write

$$\begin{aligned}
\exp \left(-\beta \sum_{i < j} \sum_{\alpha, \gamma} p_i^\alpha G_{\alpha\gamma}(\vec{r}_i, \vec{r}_j) p_j^\gamma \right) &= \prod_{i < j} (1 + f_{ij}) \\
&\simeq 1 + \sum_{i < j} f_{ij} + \dots \\
&\simeq e^{\sum_{i < j} f_{ij} + \dots}
\end{aligned} \tag{4}$$

where $f_{ij} = f(\vec{r}_i - \vec{r}_j) = \exp(-\beta \vec{p}_i \cdot \mathbf{G}_{ij} \cdot \vec{p}_j) - 1$. To lowest non trivial order in f , we get:

$$\begin{aligned}
\mathcal{Z} &= \int \prod_i d\vec{r}_i \delta(|\vec{r}_{i+1} - \vec{r}_i| - a) \exp(-\beta \mathcal{H}_{pol}(\{\vec{r}_i\})) \\
&\times \exp \left(\sum_{i < j} \int d\vec{p}_i d\vec{p}_j f_{ij} \delta(|\vec{p}_i| - p_0) \delta(\vec{p}_i \cdot (\vec{r}_{i+1} - \vec{r}_i)) \delta(|\vec{p}_j| - p_0) \delta(\vec{p}_j \cdot (\vec{r}_{j+1} - \vec{r}_j)) \right)
\end{aligned} \tag{5}$$

where $\beta \mathcal{H}_{pol} = \frac{v_0}{2} \sum_{i \neq j} \delta(\vec{r}_i - \vec{r}_j)$. Introducing the joint distribution function:

$$g(\vec{r}, \vec{u}) = \sum_i \delta(\vec{r} - \vec{r}_i) \delta(\vec{u} - \vec{u}_i) \tag{6}$$

where $\vec{u}_i = (\vec{r}_{i+1} - \vec{r}_i)/a$, the partition function (5) reads:

$$\begin{aligned}
\mathcal{Z} &= \int \mathcal{D}g \mathcal{D}\hat{g} \exp \left(i \int d\vec{r} d\vec{u} \hat{g} g - \frac{v_0}{2} \int d\vec{r} \left(\int d\vec{u} g \right)^2 \right) \\
&\times \exp \left(\frac{1}{2} \int d\vec{r} d\vec{r}' d\vec{u} d\vec{u}' g(\vec{r}, \vec{u}) V(\vec{r}, \vec{u} | \vec{r}', \vec{u}') g(\vec{r}', \vec{u}') + \log \zeta(\hat{g}) \right)
\end{aligned} \tag{7}$$

where

$$V(\vec{r}, \vec{u} | \vec{r}', \vec{u}') = \int d\vec{p} d\vec{p}' \delta(|\vec{p}| - p_0) \delta(\vec{p} \cdot \vec{u}) \delta(|\vec{p}'| - p_0) \delta(\vec{p}' \cdot \vec{u}') f(\vec{r} - \vec{r}') \tag{8}$$

and ζ is the polymeric partition function given by:

$$\zeta(\hat{g}) = \int \prod_i d\vec{r}_i \delta(|\vec{r}_{i+1} - \vec{r}_i| - a) e^{-i \sum_i \hat{g}(\vec{r}_i, \vec{u}_i)} \tag{9}$$

In the spirit of mean field or variational approaches [8], we look for a homogeneous (space independent) distribution function: $g(\vec{r}, \vec{u}) = \rho \phi(\vec{u})$, where $\rho = \frac{N}{\Omega}$ is the monomer concentration and the angular distribution function ϕ is normalized to 1. The free energy per monomer reads:

$$\beta \mathcal{F} = \int d\vec{u} \phi(\vec{u}) \log(\phi(\vec{u})) + \frac{v_0}{2} \rho - \frac{1}{2} \rho \int d\vec{u} d\vec{u}' \phi(\vec{u}) \mathcal{V}(\vec{u} \cdot \vec{u}') \phi(\vec{u}') + O(\rho^2) \tag{10}$$

where

$$\mathcal{V}(\vec{u} \cdot \vec{u}') = \int d\vec{r} d\vec{p} d\vec{p}' \delta(|\vec{p}| - p_0) \delta(\vec{p} \cdot \vec{u}) \delta(|\vec{p}'| - p_0) \delta(\vec{p}' \cdot \vec{u}') f(\vec{r}) \quad (11)$$

and the $O(\rho^2)$ term in equation (10) represents the three body repulsive interactions. Using the Onsager variational form [9]

$$\phi(\theta) = \frac{\alpha}{4\pi \sinh \alpha} \cosh(\alpha \cos \theta) \quad (12)$$

where θ is the polar angle of the unit vector \vec{u} , we obtain

$$\begin{aligned} \beta\mathcal{F} = & \log\left(\frac{\alpha}{4\pi e \tanh \alpha}\right) + \frac{2}{\sinh \alpha} \left(\arctan(e^\alpha) - \frac{\pi}{4}\right) \\ & + \frac{v_0}{2} \rho \left(1 - \frac{1}{t^2} - \frac{3}{80t^2} ((1 - 2w(\alpha))^2 + 2w^2(\alpha) - \frac{1}{3})\right) + O(\rho^2) \end{aligned} \quad (13)$$

where $t = \frac{T}{T_\theta}$, with $T_\theta = \frac{2}{3} \sqrt{\frac{a^3}{v_0}} T_D$, and $w(\alpha) = (\frac{\coth \alpha}{\alpha} - \frac{1}{\alpha^2})$. We have also assumed that $d \sim a$, i.e. that an estimate of the distance between dipoles is given by the monomer length.

Minimizing equation (13) with respect to α and ρ yields the following results:

- i) A usual second order θ -like collapse transition to a finite density phase occurs at temperature $t = 1$. Since $v_0 \sim a^3$, we have $T_\theta \sim T_D$.
- ii) In the dense phase, a discontinuous nematic-like transition occurs at temperature $t_N = \frac{T_N}{T_\theta} \simeq \frac{1}{3}$, with a small density discontinuity. Since T_N is a variational estimate, the true transition temperature is necessarily higher.

These results show that dipolar interactions are responsible for both transitions. We remind the reader that they are expected to be correct at small monomer concentration, since they rely on the virial expansion. At higher monomer concentration, one may find other phases (e.g. crystalline phases [10]). An extension of this approach to chiral chains is possible [11]. In this case, one expects to encounter a phase transition towards an inhomogeneous phase (e.g. cholesteric) at a temperature T_H higher than T_N . The possibility of a crossing between T_θ and T_H must therefore be considered. As shown in the next section, the Landau approach to the constrained dipolar chain provides a more convenient framework to study this possibility.

III. LANDAU THEORY

A. Formal developments

At a qualitative level, experimental phase diagrams are usually in agreement with the Landau theory of phase transitions. Roughly speaking, this theory, which rests over the use of symmetry arguments, may be summarized as follows

- (i) one looks for an order parameter $Q(\vec{r})$ that describes the ordered phase(s) at point \vec{r} .
- (ii) one builds a free energy density as an expansion in $Q(\vec{r})$, and in the first spatial derivatives of $Q(\vec{r})$.
- (iii) one minimizes the total free energy with respect to $Q(\vec{r})$.

This theory clearly assumes that the order parameter $Q(\vec{r})$ varies on distances much larger than the microscopic length scales. Following this line, we first soften the constraint of fixed length dipoles in equation (3) and replace it by a Gaussian constraint (the replacement of fixed length by Gaussian spins is familiar in the theory of phase transitions). We therefore have

$$\mathcal{Z}_L = \int \prod_i d\vec{r}_i d\vec{p}_i \delta(|\vec{r}_{i+1} - \vec{r}_i| - a) \frac{1}{(2\pi p_0^2)^{3/2}} e^{-\frac{\vec{p}_i^2}{2p_0^2}} \delta(\vec{p}_i \cdot (\vec{r}_{i+1} - \vec{r}_i)) \exp(-\beta\mathcal{H}) \quad (14)$$

where the subscript L on the partition function stands for Landau and the Hamiltonian \mathcal{H} is given by equation (1). Using the identity

$$\delta(\vec{y}) = \lim_{\lambda \rightarrow \infty} \left(\frac{\lambda}{2\pi} \right)^{3/2} e^{-\frac{\lambda \vec{y}^2}{2}} \quad (15)$$

we may now perform the (Gaussian) integrals over the dipole moments \vec{p}_i in equation (14). As a result, the problem now depends only on the polymeric degrees of freedom. Introducing the tensorial (order) parameter $Q_{\alpha\mu}(\vec{r})$ by

$$Q_{\alpha\mu}(\vec{r}) = \sum_i ((\vec{u}_i)_\alpha (\vec{u}_i)_\mu - \delta_{\alpha\mu}) \delta(\vec{r} - \vec{r}_i) \quad (16)$$

where the notation $\vec{u}_i = (\vec{r}_{i+1} - \vec{r}_i)/a$ was again used, we get

$$\mathcal{Z}_L = \int \prod_{(\alpha, \mu), \vec{r}} \mathcal{D}Q_{\alpha\mu}(\vec{r}) \delta \left(Q_{\alpha\mu}(\vec{r}) - \sum_i ((\vec{u}_i)_\alpha (\vec{u}_i)_\mu - \delta_{\alpha\mu}) \delta(\vec{r} - \vec{r}_i) \right) \int \prod_i d\vec{r}_i \delta(|\vec{r}_{i+1} - \vec{r}_i| - a) \exp(-\beta \mathcal{H}_{pol}) \exp\left(-\frac{1}{2} \text{Tr} \log \mathbf{B}\right) \quad (17)$$

where the matrix \mathbf{B} is defined by its matrix elements

$$B_{\alpha\gamma}(\vec{r}, \vec{r}') = \delta_{\alpha\gamma} \delta(\vec{r} - \vec{r}') + \beta p_0^2 \sum_{\mu} Q_{\alpha\mu}(\vec{r}) G_{\mu\gamma}(\vec{r}, \vec{r}') \quad (18)$$

Using the identity

$$\delta(Q_{\alpha\mu} - d_{\alpha\mu}) = \int \frac{\mathcal{D}\hat{Q}_{\alpha\mu}}{2\pi} \exp i \hat{Q}_{\alpha\mu} (Q_{\alpha\mu} - d_{\alpha\mu}) \quad (19)$$

one may write

$$\mathcal{Z}_L = \int \prod_{(\alpha, \mu), \vec{r}} \mathcal{D}Q_{\alpha\mu}(\vec{r}) \mathcal{D}\hat{Q}_{\alpha\mu}(\vec{r}) \exp(i \int d\vec{r} \sum_{\alpha \leq \mu} Q_{\alpha\mu}(\vec{r}) \hat{Q}_{\alpha\mu}(\vec{r})) \exp(-\beta \mathcal{H}_{pol}(\mathbf{Q})) \exp\left(-\frac{1}{2} \text{Tr} \log \mathbf{B}\right) \exp(\log \zeta(\hat{\mathbf{Q}})) \quad (20)$$

with

$$\zeta(\hat{\mathbf{Q}}) = \int \prod_i d\vec{r}_i \delta(|\vec{r}_{i+1} - \vec{r}_i| - a) \exp \left(-i \sum_{\alpha \leq \mu} \sum_i \hat{Q}_{\alpha\mu}(\vec{r}_i) ((\vec{u}_i)_\alpha (\vec{u}_i)_\mu - \delta_{\alpha\mu}) \right) \quad (21)$$

and where we have expressed \mathcal{H}_{pol} as a function of \mathbf{Q} (see equation (23) below). So far, no approximations beside the assumption of a Gaussian distributed length of the dipoles were made. We stress the fact that the number of independent variables $\hat{Q}_{\alpha\mu}(\vec{r})$ is equal to six, since \mathbf{Q} is a symmetric rank 2 tensor. This is why the sum over the components (α, μ) in equations (20, 21) is restricted to $\alpha \leq \mu$.

B. The physical order parameters

At this stage, it may be useful to establish the relation of the previous section with the virial approach. It is clear that the tensor (or matrix) $\mathbf{Q}(\vec{r})$ can also be expressed through the joint distribution function of equation (6) as

$$Q_{\alpha\mu}(\vec{r}) = \int d\vec{u} \, g(\vec{r}, \vec{u}) ((\vec{u})_\alpha (\vec{u})_\mu - \delta_{\alpha\mu}) \quad (22)$$

Furthermore, one may build from $\mathbf{Q}(\vec{r})$ a (scalar) density

$$\rho(\vec{r}) = -\frac{1}{2} \text{Tr} \, \mathbf{Q}(\vec{r}) \quad (23)$$

and a traceless tensor

$$\mathbf{q}(\vec{r}) = \mathbf{Q}(\vec{r}) - \frac{\mathbf{I}}{3} \text{Tr} \, \mathbf{Q}(\vec{r}) \quad (24)$$

where \mathbf{I} is the unit tensor. Assuming that both quantities are space independent, we easily recover the results of section II. For space dependent order parameters, the Landau-Ginzburg free energy density $\mathcal{F}_L(\vec{r})$ is defined by:

$$\mathcal{Z}_L = \int \mathcal{D}\rho(\vec{r}) \mathcal{D}q_{\alpha\mu}(\vec{r}) e^{-\beta \int d\vec{r} \mathcal{F}_L(\vec{r})} \quad (25)$$

It can be evaluated by

- (i) performing a saddle point method on $\hat{\mathbf{Q}}$ in equation (20) and replacing $\hat{\mathbf{Q}}$ as a function of \mathbf{Q} .
- (ii) expanding the resulting free energy density in the exponent of (20) in powers of \mathbf{Q} and performing a local gradient expansion. Note that all terms of the expansion could have been obtained from symmetry considerations.
- (iii) expressing the free energy density in terms of $\rho(\vec{r})$ and $\mathbf{q}(\vec{r})$.

The resulting Landau free energy density reads:

$$\begin{aligned} \mathcal{F}_L(\vec{r}) = & \frac{a_0^2}{2} (\nabla \rho(\vec{r}))^2 + \frac{a_2}{2} (T - T_\theta) \rho^2(\vec{r}) + \frac{a_3}{3} \rho^3(\vec{r}) + \dots \\ & + \frac{b_0}{2} \partial_\alpha q_{\alpha\mu}(\vec{r}) \partial_{\alpha'} q_{\alpha'\mu}(\vec{r}) + \frac{b'_0}{2} \partial_\gamma q_{\alpha\mu} \partial_\gamma q_{\alpha\mu} + \frac{b_2}{2} (T - T_0) \text{Tr} \, \mathbf{q}^2(\vec{r}) \\ & - \frac{b_3}{3!} \text{Tr} \, \mathbf{q}^3(\vec{r}) + \frac{b_4}{4!} (\text{Tr} \, \mathbf{q}^2(\vec{r}))^2 + \dots \\ & + \frac{c_0}{2} \rho(\vec{r}) \partial_{\alpha\mu}^2 q_{\alpha\mu}(\vec{r}) - \frac{c_1}{2} \rho(\vec{r}) \text{Tr} \, \mathbf{q}^2(\vec{r}) + \dots \end{aligned} \quad (26)$$

where we use the standard summation over repeated indices. The various coefficients a, b, c in (26) can in principle be calculated using the method described above. In particular, the temperature T_θ is the same as that defined in section II and T_0 would be the nematic transition temperature if there was no cubic term in \mathbf{q} in equation (26).

C. Including chirality

The observation that the backbone of proteins has chirality can be appreciated through the Ramachandran plot [1]. The chirality of the C_α “virtual chain” is predominantly associated with the ϕ dihedral angles. It is not easy to take chirality into account at a microscopic level [12], while it is so at a Landau-like level [13], since then, only very general symmetry considerations matter. In particular, if the system is described by a tensor $\mathbf{q}(\vec{r})$, the absence of inversion symmetry ensures that a new (scalar) invariant shows up in equation (26), namely

$$\mathcal{F}_{chiral}(\vec{r}) = D \epsilon_{\alpha\mu\nu} q_{\alpha\delta} \partial_\mu q_{\nu\delta} \quad (27)$$

where D is a measure of the strength of the chirality and $\epsilon_{\alpha\mu\nu}$ the antisymmetric third rank tensor. The full Landau free energy density $\mathcal{F}_L^{tot}(\vec{r})$ of the constrained dipolar chiral chain then reads

$$\mathcal{F}_L^{tot}(\vec{r}) = \mathcal{F}_L(\vec{r}) + \mathcal{F}_{chiral}(\vec{r}) \quad (28)$$

where $\mathcal{F}_L(\vec{r})$ and $\mathcal{F}_{chiral}(\vec{r})$ are given respectively in equations (26) and (27). It is clear that equation (28) describes the coupling between a usual θ collapse described by $\rho(\vec{r})$ and blue phase-like ordering [14] described by $\mathbf{q}(\vec{r})$. For our purposes, it is important to note that equation (27) implies that a modulated order in $\mathbf{q}(\vec{r})$ sets in at a temperature T_χ which is higher [14,15] than the temperature T_N of the uniform (nematic) order; on the other hand equation (26) shows that, to lowest order, the θ collapse occurs at the same D -independent temperature T_θ . Before exhibiting the crossing of the two temperatures T_χ and T_θ in a specific case, we briefly summarize the existing state of the art for blue phases.

D. Summary of the blue phases folklore

In chiral systems, the blue phases (BP) may show up in a narrow temperature range ($\leq 1\text{K}$) between the simple cholesteric (helical) liquid crystal phase and the isotropic liquid. Their theory is quite complicated [14,15]; their ordering is described by a symmetric rank 2 tensor which can, in some appropriate limits, be linked to the molecular orientations. So far two crystalline phases (BP I, BP II) and one non-crystalline phase (BP III) have been found. More complicated phases may exist when an electric field is present.

The crystalline phases are characterized by a body centered (BP I) or simple cubic (BP II) lattice. The unit cell contains of the order of 10^7 molecules, so that the Landau expansion may be a priori trustworthy. Note that these crystalline structures are threaded by disclinations (line defects of the molecular orientations).

The non crystalline phase (BP III) is of particular interest [16]. It has the same macroscopic symmetry as the isotropic liquid, and the (BP III)-(isotropic liquid) phase transition has a critical end point, much like the liquid-gas transition. Furthermore, attempts have been made to describe this phase as resulting from an unstable localized mode (see the references in [14]), as opposed to an extended mode for the crystalline BP's.

IV. A SIMPLE EXAMPLE OF ANISOTROPIC COLLAPSE

We will exhibit, in a simple way, the crossing between the θ (uniform) collapse temperature T_θ and the temperature T_χ below which a modulated order sets in. Following references [15,17], we consider in equation (28) the appearance of helicoidal order in the tensor $\mathbf{q}(\vec{r})$. At this point, it is perhaps useful to recall the reader that the various “helices” of this section are not the α -helices present in proteins. Indeed, these “helices” are linked to the order parameter of equation (24), and, as in all polymeric problems, it is difficult to deduce the chain configuration(s) from the physical order parameter(s). The $\mathbf{q}(\vec{r})$ helicoidal order is described by:

$$q_{\alpha\mu}(\vec{r}) = q_{\alpha\mu}(z) = \frac{1}{\sqrt{6}} q \sin \phi M_{\alpha\mu} + \frac{1}{\sqrt{2}} q \cos \phi N_{\alpha\mu}(z) \quad (29)$$

where the matrices \mathbf{M} and $\mathbf{N}(z)$ are given by

$$\mathbf{M} = \begin{pmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & -2 \end{pmatrix} \quad (30)$$

and

$$\mathbf{N} = \begin{pmatrix} \cos k_0 z & \sin k_0 z & 0 \\ \sin k_0 z & -\cos k_0 z & 0 \\ 0 & 0 & 0 \end{pmatrix} \quad (31)$$

where $\vec{k}_0 = \frac{D}{b'_0} \vec{e}_z$ is the wave vector of the modulation. Usual cholesteric order (i.e. the “uniaxial” helix) corresponds to $\phi = \frac{\pi}{6}$, while the purely biaxial helix is described by $\phi = 0$.

We insert this trial order parameter in equation (28) and get:

$$\begin{aligned} \mathcal{F}_L^{tot}(\vec{r}) &= \frac{a_0^2}{2} (\nabla \rho(\vec{r}))^2 + \frac{a_2}{2} (T - T_\theta) \rho^2(\vec{r}) + \frac{a_3}{3} \rho^3(\vec{r}) + \dots \\ &+ (b_2(T - T_0) - c_1 \rho(\vec{r})) \frac{q^2}{2} - \frac{b_3}{\sqrt{6}} \sin 3\phi \frac{q^3}{6} + b_4 \frac{q^4}{24} + \dots \\ &- \frac{D^2}{2b'_0} q^2 \cos^2 \phi \end{aligned} \quad (32)$$

This free energy density is to be minimized with respect to q, ϕ and $\rho(\vec{r})$. Of particular importance are the terms which couple the order parameters in (28). With our choice of the order parameter $q_{\alpha\mu}(z)$, the first non zero term corresponds to the c_1 coefficient of equation (26). Moreover, on physical grounds, this coefficient must be positive, since an increase of the density is expected to favor the appearance of a liquid crystal type of ordering. Furthermore, the order in $\rho(\vec{r})$ can be shown to be uniform ($k = 0$ ordering). Due to the large number of coefficients in the free energy density, it is appropriate to work with dimensionless quantities, and we shall follow the notations of reference [15]. The rescaled total free energy per unit volume f reads:

$$\begin{aligned} f &= \frac{1}{4} (t - \alpha c) Q^2 - \frac{1}{4} \kappa^2 Q^2 \cos^2 \phi \\ &- Q^3 \sin 3\phi + Q^4 + \frac{1}{2} t' c^2 + c^3 \end{aligned} \quad (33)$$

with

$$q = \frac{4}{\sqrt{6}} \frac{b_3}{b_4} Q, \quad \rho = \frac{2}{3} \frac{b_3^{4/3}}{b_4 a_3^{1/3}} c, \quad (34)$$

$$t = \frac{1}{\delta}(T - T_0), \quad t' = \gamma(T - T_\theta), \quad (35)$$

$$\gamma = \frac{3}{2} \frac{a_2 b_4}{a_3^{2/3} b_3^{4/3}}, \quad \delta = \frac{b_3^2}{18 b_2 b_4} \quad (36)$$

$$\kappa = 18 k_0^2 \frac{b_4 b'_0}{b_3^2}, \quad c_1 = \frac{b_3^{2/3} a_3^{1/3}}{12} \alpha, \quad (37)$$

and

$$\mathcal{F}_L^{tot} = \left(\frac{3}{2}\right)^3 \frac{b_4^3}{b_3^4} f, \quad (38)$$

We just quote here the conclusions of a study of equation (33). Technical details will appear elsewhere [18]. The phase diagram can be studied in the (temperature, chirality) plane. For high enough values of the chirality parameter κ ,

$$\kappa^2 \left(1 - \frac{\alpha^2}{32\gamma(\delta\kappa^2 - (T_\theta - T_0))}\right) > 9 \quad (39)$$

we get a continuous transition towards a biaxial helix at a reduced temperature $t_\chi = \kappa^2$ corresponding to a real temperature

$$T_\chi = T_0 + \delta\kappa^2 \quad (40)$$

Below the transition, the reduced density grows as $c \simeq Q^2$. The low temperature phase can be viewed as a compact phase with helical order. From a protein-oriented point of view, this would correspond to a direct transition from a coil state (denatured) to a native state (i.e. compact with secondary structures).

At much lower chirality, when $T_\chi < T_\theta$, the scenario is more like the one in section II: there is first a θ collapse transition at $t'_\theta = 0$, followed at a lower temperature by a discontinuous transition towards a “uniaxial” helix.

At intermediate chiralities, several phase diagrams are possible, depending on the relative values of the parameters. In particular, the location of the phase transition between the compact modulated phases (biaxial and uniaxial) is very model dependent.

In figure 1, we display a plausible phase diagram.

V. CONCLUSION

Using the fact that dipolar interactions imply the existence of a tensorial order parameter (see equation (16)), we have shown that chiral chains may have isotropic (θ -like) or anisotropic (blue phase -like) collapse transitions. This result was found in a simple model with helicoidal order. The connexion with blue phases is perhaps not very surprising since the molecules of some of these compounds have dipoles perpendicular to the molecular axis. It is clear that the same questions that arise in the study of blue phases should arise, *mutatis mutandis*, in the study of chiral dipolar chains:

- (i) For very chiral systems, is the continuous transition towards the compact biaxial phase preempted by a discontinuous transition to a compact phase with a (hexagonal, body-centered cubic,...) superposition of biaxial helices?
- (ii) Can one find a description of low chirality systems in terms of double twist cylinders?
- (iii) Can one link the order in $\mathbf{q}(\vec{r})$, the chain configuration(s) and the dipole configuration(s)? Does a crystalline order in $\mathbf{q}(\vec{r})$ imply the existence of defects in the orientation of the chain ?

The application of the previous results to (bio)polymers can be roughly summarized as follows. Since we are concerned with collapsed phases with uniform density, we are typically in a melt situation. The study of a single chain (such as a protein) is presently out of reach. In both cases, a more detailed analysis requires a better experimental knowledge of the various parameters (chirality,...). Nevertheless, we think that our approach is useful for the protein folding problem. In particular [18], one may look for a double twist interpretation of α -helices and β -sheets, the possible existence of localized instabilities (such as the ones in BP III [19]) and their implications for the folding process. Along these lines, it is reassuring (although not completely unexpected) to note that the secondary structures of real proteins are well characterized by a $\mathbf{q}(\vec{r})$ tensorial order parameter [20].

We thank Marc Delarue, Jean-Renaud Garel, Roland Netz and Paweł Pieranski for pleasant and stimulating discussions.

Figure caption: Schematic phase diagram of the model in the (temperature, chirality) plane. The phases are labelled by C (coil), IG (isotropic globule), AG_1 and AG_2 (anisotropic globules). The $C - IG$ transition, and the $C - AG_2$ transition (for large enough chirality), are continuous.

REFERENCES

- [1] T.E. Creighton, *Proteins*, W.H. Freeman, New York (1984).
- [2] T.E. Creighton (editor), *Protein Folding*, W.H. Freeman, New York (1992).
- [3] K.A. Dill, S. Bromberg, K. Yue, K.M. Fiebig, D.P. Yee, P.D. Thomas and H.S. Chan, *Protein Science*, **4**, 561 (1995).
- [4] L. Pauling and R.B. Corey, *Proc. Natl. Acad. Sci. (USA)*, **37**, 235, 251, 272, 729 (1951).
- [5] T. Garel, H. Orland and E. Pitard, “Protein folding and heteropolymers” , Saclay preprint T97-003, to appear in *Spin Glasses and Random Fields*, A.P. Young (ed.), World Scientific, Singapore (1997).
- [6] S. Doniach, T. Garel and H. Orland, *J. Chem. Phys.*, **105**, 1601 (1996).
- [7] B. Honig and A. Nicholis, *Science*, **268**, 1144 (1995).
- [8] G.J. Vroege and H.N.W. Lekkerkerker, *Rep. Prog. Phys.* **55**, 1241 (1992) and references therein.
- [9] L. Onsager, *Ann. NY Acad. Sci.* **51**, 627 (1949).
- [10] B. Groh and S. Dietrich, *Phys. Rev. E*, **54**, 1687 (1996) and references therein.
- [11] J.P. Straley, *Phys. Rev. A*, **14**, 1835 (1976).
- [12] A.B. Harris, R.D. Kamien and T.C. Lubensky, *Phys. Rev. Lett.*, **78**, 1476 (1997).
- [13] P.G. de Gennes and J. Prost, *The Physics of Liquid Crystals*, O.U.P, Oxford (1996).
- [14] D.C. Wright and N.D. Mermin, *Reviews of Mod. Phys.*, **61**, 385 (1989).
- [15] H. Grebel, R.M. Hornreich and S. Shtrikman, *Phys. Rev. A*, **28**, 1114 (1983).
- [16] T.C. Lubensky and H. Stark, *Phys. Rev. E*, **53**, 714 (1996) and references therein.

- [17] S.A. Brazovskii and S.G. Dmitriev, Sov. Phys. JETP, **42**, 497 (1976).
- [18] E. Pitard, T. Garel and H. Orland, in preparation.
- [19] R.M. Hornreich, M. Kugler and S. Shtrikman, Phys. Rev. Lett., **48**, 1404 (1982).
- [20] Marc Delarue et al., in preparation.

